REMARKS

1. Claims

Claims 1-16, 18-23, 29 and 53-64 are currently pending. Claims 16, 54, 56, 61 and 64 have been amended to address 35 U.S.C. §112, second paragraph rejections. No Previously Presented matter has been added.

2. Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 16, 54, 56, 61 and 64 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner has rejected claims 16, 54, 56 and 61 for lack of antecedent basis for the phrase "GDF-8 and a subsequence thereof". Applicant has deleted this phrase from the rejected claims to obviate the rejection. The Examiner had also rejected claim 64 for lack of clarity. Applicant has amended the claim so that it is now clear that the modification is made by inserting at least one foreign T-helper cell epitope in one or more of the recited first amino acid sequences of SEQ ID NO: 12. Applicant believes that the foregoing claim amendments have overcome the Examiner's indefiniteness rejections and respectfully requests reconsideration and removal of the rejections.

3. Rejections under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-2, 16, 19-23, 29, 53-54, 56, 58 and 60-64 under 35 U.S.C. §103(a) as being unpatentable over Barker et al. (U.S. Patent No. 6,369,201) and in view of the known facts disclosed in the Specification at page 16, lines 24-30. The Examiner argues that Barker teaches a method for in vivo down-regulation of myostatin activity, which will result in an increase in the muscle mass of an animal, which comprises administering at least one full length myostatin polypeptide, or at least one myostatin analogue, wherein myostatin is derived

from bovine and myostatin immunoconjugate comprising at least one myostatin polypeptide linked to an immunological carrier. The Examiner explicitly acknowledges that Barker fails to teach inserting a P2 or P30 *Tetanus toxoid* epitope into the myostatin polypeptide or, indeed, where such modifications could be made. Yet, the Examiner still concludes that it would have been "obvious, conventional and within the skill of a person of ordinary skill in the art at the time the invention was made *to identify the exact position for substitution of the Tetanus toxoid epitope in the myostatin molecule in order to facilitates breaking autotolerance of said molecule . . ." (emphasis added).* In essence, the Examiner argues that despite the lack of teaching in Barker, the skilled artisan would be able to deduce exactly where modifications (i.e. the insertion of foreign T-helper cell epitopes) could be made in the myostatin molecule without destroying its immunogenicity. Applicant strongly disagrees.

The Examiner fails to identify any reference that teaches or remotely suggests that modifications could be made in the specific portions of the peptide identified by the inventors of the present application. Although Barker discloses a method for in-vivo down-regulation of myostatin and the linking of an "immunological carrier", such as tetanus to a myostatin molecule, it does not teach modifying a myostatin molecule by inserting a foreign T-helper cell epitope such as the P2 or P30 Tetanus toxoid epitope. The only portion of the Barker reference which discusses preparing modified myostatin molecules merely relates to performing amino acid deletions, substitution and/or additions while maintaining a certain percent identity with the native polypeptide (see generally cols. 6-7 of Barker). This in no way suggests that foreign T-helper epitopes could be inserted into defined portions of the myostatin polypeptide.

As attested to in the attached Declaration under 37 C.F.R. §1.132 of Dr. Steen Klysner, a person of ordinary skill in the art, it would not have been obvious, conventional and within the skill of an ordinary person in the art at the time the invention was made to determine the exact position for substitution of the *Tetanus toxoid* epitope in the myostatin peptide in order to facilitate the breaking of auto-tolerance. While the general concepts of inducing antigenicity and breaking autotolerance were known in the art, in Dr. Klysner's opinion, the teachings within the art, the general disclosure at page 16, lines 24-30 of the Specification and the teachings of the Barker reference would not provide the skilled artisan with the necessary information to identify

the exact positions for substitution because numerous factors must be taken into account to ensure that the invention will work for its desired purpose. Specifically, the skilled artisan would have to ensure that the modifications produced the desired immunogenic effect; would be properly presented and recognized by the animal's immune system; would maintain the overall secondary, tertiary and quaternary structure of the peptide and would conserve a substantial portion of the B-cell epitopes found in the native peptide. Determining exactly where the peptide could be modified, therefore, necessitated much investigation and experimentation. In fact, the present inventors had to conduct a series of complex sequence and structure analyses from the spring of 1999 through the summer of 2000 to determine which portions of the native myostatin peptide were best suited for modification.

Based on the foregoing remarks and the Declaration of Dr. Klysner, it is clear that the teachings in the prior art would not enable the skilled artisan to identify the exact positions for modification described in the present application but merely represent an invitation to experiment. Thus, Applicant submits that the present invention is, in no way, suggested or rendered obvious in view of the Barker reference or the general disclosure on page 16 of the present application. As such, Applicant respectfully requests reconsideration and removal of the obviousness rejection.

4. Rejection under 35 U.S.C. §112, first paragraph

Finally, the Examiner has rejected claims 1-2, 16, 19-23, 53-54, 58 and 60-64 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that this is a "New Matter" rejection. Applicant respectfully traverses.

The rejected claims were amended in the last response to specifically define how the GDF-8 polypeptide could be modified. The claims are presently directed to a modified myostatin peptide wherein at least one foreign T-helper cell epitope is inserted into one or more of residues 1-12, 18-41, 43-48, 49-69 or 79-104 in SEQ ID NO: 11 or 12. This amendment finds

clear support in the Specification. The paragraph bridging pages 28-29 specifically states that " . . . modification in at least one of the following subsequences of C-terminal GDF 8 will result in suitable immunogenic molecules: Residues 18-41, 49-69 or 79-104 in SEQ ID NO: 11 or 12, or corresponding subsequences from GDF-8 polypeptide of different origin than human, bovine, porcine, chicken or turkey . . .". The Specification goes on to state that " . . .[A]lso insertion (or substitution) into any one of the loop areas or the flexible termini (residues 1-12, 18-30, 42-51, 82-86 and 105-109) of the C-terminal GDF-8 fragment is preferred. Applicant would also like to point out that support for the claims as amended may be found in original claim 17 and also in SEQ ID NO: 23 (discussed on page 56) which relates to a variant wherein more than one area of the GDF-8 polypeptide has been modified. The Specification, therefore, clearly describes a GDF-8 polypeptide which can be modified as described in claims 1-2, 16, 19-23, 53-54, 58 and 60-64.

In view of the foregoing comments, Applicant has not amended the claims in the manner suggested by the Examiner. Applicant submits that the Specification provides adequate written description support for claims 1-2, 16, 19-23, 53-54, 58 and 60-64 and accordingly requests reconsideration and removal of the 35 U.S.C. §112, first paragraph rejection.

Examination on the merits and favorable action and allowance of all the claims are requested.

If the Examiner has any questions concerning this application, he is requested to contact Leonard Svensson (Reg. No.: 30,330) the undersigned at (714) 708-8555 in California.

Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicant hereby petition for an extension of two (2) months to March 21, 2004 (Sunday), for the period in which to file a response to the Office Action dated October 21, 2003.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Enclosure: Declaration under 37 C.F.R. 1.132 of Dr. Steen Klysner

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